HOMBERGER

Molecular Rearrangements In the Camphor and Fenchone Series

CHEMISTRY

Ph. D.

1910

UNIV OF
ILLINOIS
LIBRARY

UNIVERSITY OF ILLINOIS
LIBRARY

Class 1910 Book H75 Volume

Digitized by the Internet Archive
in 2013

http://archive.org/details/molecularrearran00homb

MOLECULAR REARRANGEMENTS IN THE CAMPHOR AND FENCHONE SERIES

8 79
10 9 w 1/4

BY

ALFRED WILHELM HOMBERGER

A. B. University of Wisconsin, 1905
A. M. University of Illinois, 1908

THESIS

Submitted in Partial Fulfillment of the Requirements for the

Degree of

DOCTOR OF PHILOSOPHY

IN CHEMISTRY

IN

THE GRADUATE SCHOOL

OF THE

UNIVERSITY OF ILLINOIS

1910

1910
H75

1910
H75

14 Sio Binding 1 05

UNIVERSITY OF ILLINOIS

THE GRADUATE SCHOOL

May 25, 1910

I HEREBY RECOMMEND THAT THE THESIS PREPARED UNDER MY SUPERVISION BY

Alfred Wilhelm Homberger

ENTITLED Molecular Rearrangements in the Camphor and Fenchone Series

BE ACCEPTED AS FULFILLING THIS PART OF THE REQUIREMENTS FOR THE

DEGREE OF Doctor of Philosophy

W. A. Noyes.
In Charge of Major Work

W. A. Noyes.
Head of Department

Recommendation concurred in:

Committee on Final Examination

204840

UIUC

The following work was undertaken in the Chemical Laboratory of the University of Illinois at the suggestion of Professor W. A. Noyes. The work was begun in the fall of 1907, but discontinued in 1908, when the relations of Camphor to Fenchone were studied in the University of Göttingen, Germany, with Professor Otto Wallach. The work was resumed at the University of Illinois in the fall of 1909.

I wish to take this opportunity to express my most hearty and sincere thanks to Professor W. A. Noyes for the untiring inspiration and constant support which he has given me in the experimental part of this work.

MOLECULAR REARRANGEMENTS IN THE CAMPHOR AND FENCHONE SERIES.

Introduction.

No molecule has ever occasioned the amount of thought or given rise to such a variety of formulas as the camphor molecule. The relations of the atoms in this molecule have been discussed since the setting up of the brutto-formula by Dumas in 1833. From that time until 1893 when Bredt set up his formula, a framework was sought which would explain all the complex derivatives of camphor and yet take for granted as few rearrangements as possible. To-day, in spite of the increased derivatives, with their attendant complexities, the number of deviations from Bredt's formula has been increased. These deviations can be explained only on the basis of molecular rearrangements.

The passing over of camphor into m-cymene, the formation of tetra- and hexahydro-m-xylene under the influence of hydriodic acid on camphoric acid, the passing over of the camphoroxime into the α-campholenic acid, and α-campholenic acid into β-campholenic acid, the distillation of the calcium salts of the α- and β-nitrilic acids are to be sure no simple reactions and can be explained only by molecular rearrangements. However, not all the knowledge of the configurations of this series has come from a study of its derivatives. Fenchone, which like camphor has a five-ring, and pinene, which has a four-ring, have aided largely in giving a clearer insight into the molecule.

In many of the cases cited above, an immediate relation cannot be traced to the original molecule. If, however, similar rearrangements are found in cases outside of the camphor and fenchone series there is all the more reason

why the more numerous complexities found in these series should be explained on a similar basis.

Taking for granted rearrangements in these molecules and the possibility that they occur more easily and more frequently here than in numerous other organic molecules, it is essential that the factors which bring about these rearrangements be sought, as well as, the interpretation of the mechanism thereof. Some such causes have been already attributed to

(a) elevated temperature, Pinene to Dipentene[1],

(b) mineral acids, α- Isofenchonoxime to β-Isofenchonoxime[2], Isofencholenyl alcohol to Fenchenole[3],

(c) alkalis, the work of Brykner in transforming the isoborneol into borneol in xylene by means of sodium[4] might be placed parallel here to the conversion of the α- thujone into β-thujone[5], Pinene to Dipentene[6], Isofencholenyl alcohol to Fenchenole[7], α- Isofenchonoxime to β- Isofenchonoxime[8].

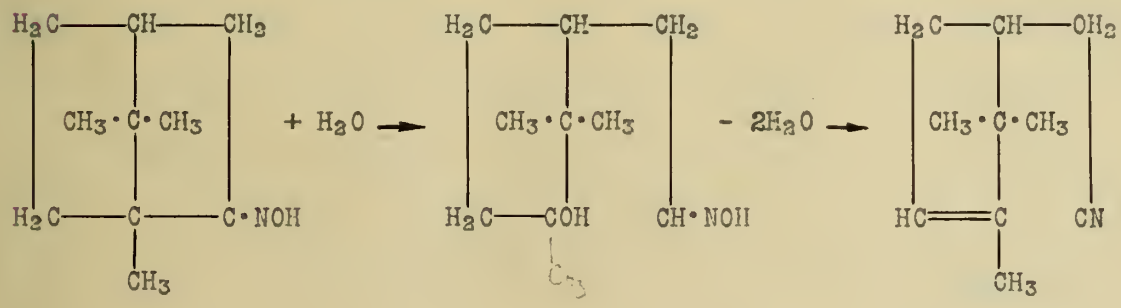
Wallach in the study of oximes[9] of the most simple saturated ketones in the terpene series has found that the isomerizations run parallel to the Beckmann scheme, that is, the nitrogen forces itself between two carbon atoms to form the NH group, thereby yielding a lactam. Beckmann[10] gives such an interpretation with regard to the product of rearrangement of menthoneoxime and Bredt[11] has pointed out a similar Beckmann's rearrangement in the formation of

- -

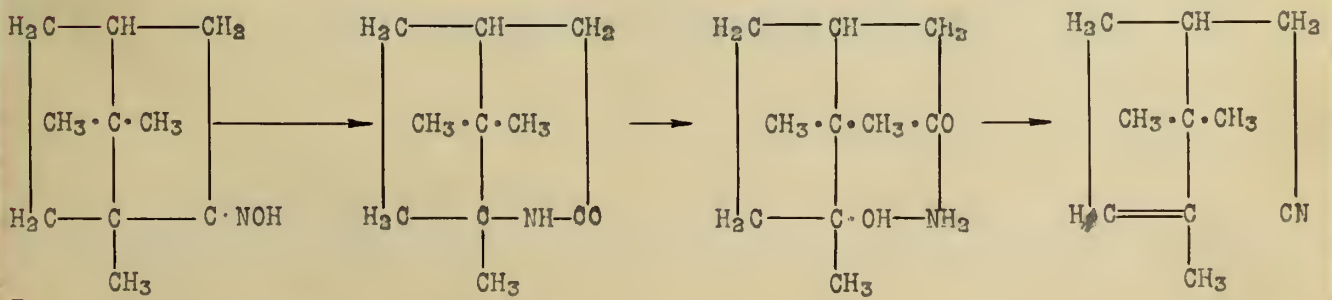
1. Ann. 227, 282, 288, 289, 290 (1885); 230, 225-272 (1885); 239, 1-54 (1887)
2. Ibid., 269, 332 (1892).
3. Ibid., 284, 338 (1895).
4. Ibid., 340, 19 (1905); J. russ. chem. Ges. 35, 537.
5. Ann. 336, 252-257 (1904).
6. Ibid., 227, 284, 285, 286 (1885).
7. Ibid., 284, 338 (1895).
8. Ibid., 269, 332 (1892).
9. Ibid., 309, 5 (1899).
10. Ibid., 289, 390 (1896).
11. Ber. 26, 305 (1893); Ann. 289, 15 (1896).

the camphonitrile. Wallach[1] in working with the oximes of the cyclic ketones attempted to offer an interpretation for the mechanism of the rearrangement which would include the lactam formation and also the isomerisation of such compounds as carvoxime to carvolene-thymol and of the isocarvoxime to carvolene. He shows how in the lactam formation the cyclic oximes are transformed into lactams and in the other case into bases or hydroxybases. The first type, a frequent case, is the ordinary Beckmann's rearrangement. Wallach's interpretation of the second type of rearrangement is that in the case of the oximes the hydroxylof the oxime group unites with a labile hydrogen atom and goes off as water. Such systems are not stable under all conditions but will take up water again, causing a splitting open of the ring and the formation of a new molecular structure.

Wallach's rearrangement for camphoroxime is



Beckmann's rearrangement for camphoroxime is



1. Ann. 346, 266 (1906).

A glance at the history of camphor and fenchone and some of their derivatives may lead to a clearer understanding of these complex molecules, as well as, show that their structure can only be explained by molecular rearrangements.

Historical Review.

Since the latter part of the 18th century, camphor has been a problem of investigation. The first work, worthy of mention, that has been done on camphor, seems to have been done by Rosegarten in 1785,[1] when he attempted to withdraw the phlogiston by repeated treatment with nitric acid, and obtained a peculiar acid greatly resembling and yet differing from oxalic acid. Dörfurth in 1793[2] declared this acid identical with benzoic acid. Later, in 1809, von Buchloz pointed out its peculiar properties. Malagati, Laurent, Gay-Lussac and Liebig about 1830 established the composition of the molecule. Until this time the work was almost entirely on the physical properties of camphor.

As to the inner structure of the molecule Dumas in 1833[3] set up the brutto-formula for camphor. Freing[4] by distillation with lime obtained camphorone and a naphthalene. Berthelot in 1859[5] succeeded in passing from camphor to borneol. The reverse, borneol to camphor, had been known since 1840. These are really the first rearrangements in the series.

Until 1893 all the camphor formulas aimed principally to show the relation of camphor to p-cymene (p-methylisopropyl benzene), and its hydroxyderivative, carvacrol, on the one side, and the terpenes on the other. Little

1. Dissertation in Göttingen.
2. Abhandlung über Kampfer.
3. Ann. 6, 245; 48, 430.
4. Ibid. 15, 286.
5. Ibid. 110, 368 (1859).

significance was attached to the fact that although the above named products were fairly stable toward a few reagents they would easily be rearranged by others, as well as, by higher temperatures. Not until a work by Fittig, Köbrich, and Jilke[1] in 1869 was mention made of other products. Upon treatment of camphor with molten zinc chloride they obtained toluene, xylene, pseudocumene and laurene in addition to the hydrocarbon, cymene. These occured in such quantities that they could no longer be regarded as side-products.

Armstrong and Miller working at low temperatures obtained by splitting water out of camphor m-cymene, asymmetric ethyl-o-xylene and small quantities of tetramethyl-benzene. These investigators by heating camphor with iodine also obtained carvacrol, dimethyl-ethyl benzene, tetramethyl-benzene and a hydrocarbon $C_{10}H_{20}$.

Tollens and Fittig[2] and Weyl[3] were the first to come to the conclusion that camphor was a ketone. Although Weyl's early conclusions as to the structure of camphor were quite correct, his conclusions for the constitution of the acid were wrong. He inferred from his observations that it was a mono-basic acid. It must be remembered, however, that molecular rearrangements in this series by means of acid reagents were not known at that time and the molecule was conceived in many different ways by such men as Weyl[4], Berthelot,[5] and Kachler[6]. Finally Victor Meyer[7] comes to view the molecule entirely differently with regard to its constitution. He concluded that the acid was bibasic, which conclusion could also have been drawn from the work of Moitessier[8]. Victor

---

1. Ann. chem. Pharm. 145, 129.
2. Ibid. 129, 371 (1864).
3. Ber. 1, 94 (1868).
4. Ibid. 1, 94 (1868).
5. Jahrb., 334 (1869).
6. Ann. 159, 281.
7. Ber. 3, 116 (1870).
8. Jahrb. 1866, 410.

Meyer emphasized its transformation into cymene and its non-reducibility with sodium amalgam.

The production of artificial camphor dates back to 1841, when it was obtained by von Pelonze by oxidation of borneo-camphor and by von Gerhardt and Cahours out of the Baldrian-oil. The latter product proved to be identical with our borneol. Later Berthelot[1] converted camphene by way of platinum-black and 1868 by oxidation with chromic acid. Today, it is generally accepted that in the oxidation of this camphene to camphor, the first product formed is isoborneol, which by further oxidation is converted into camphor. That such an intermediate reaction takes place was first shown by Montgolfier in 1876, von Haller in 1889, and Bertram and Walbaum in 1894.

The work of Haller[2], and von Rosenberg[3] lead Komppa[4] to set up a total synthesis of camphoric acid, which is one of the most beautiful pieces of work of modern chemistry.

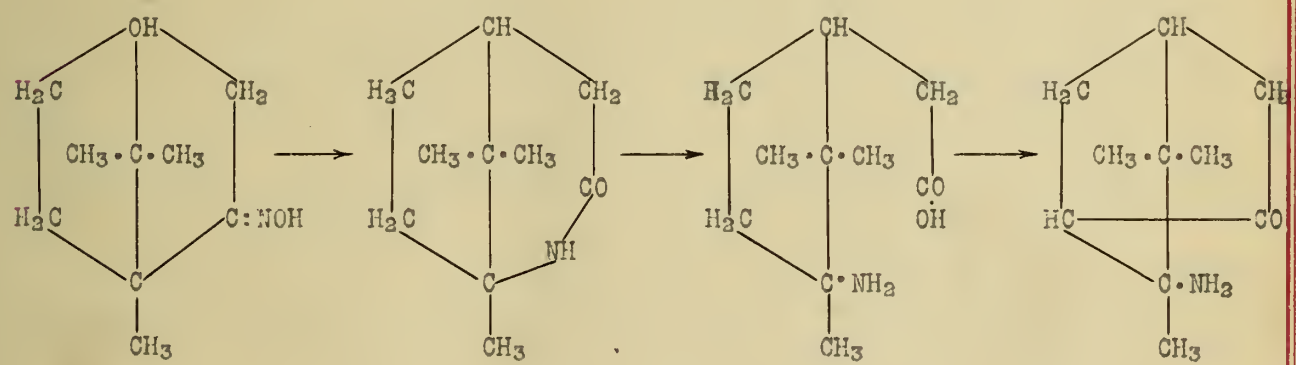
The variety of formulas set up for camphor was due to the difficulty in satisfactorily tracing a number of the reactions to the mother molecule. The reactions were unusual in that there seemed to be wanderings of carbon groups within the pentamethylene ring of the camphoric acid. The peculiarity of some of these reactions could be explained only by rearrangements. A few of these reactions will serve to show the cause of early wrangling concerning these molecules.

Wreden[5] in 1877 observed a rearrangement produced by the action of hydriodic acid on camphoric acid. He obtained tetra- and hexahydro-m-xylene. Wallach[6] in 1892 did some further work on this reaction.

---

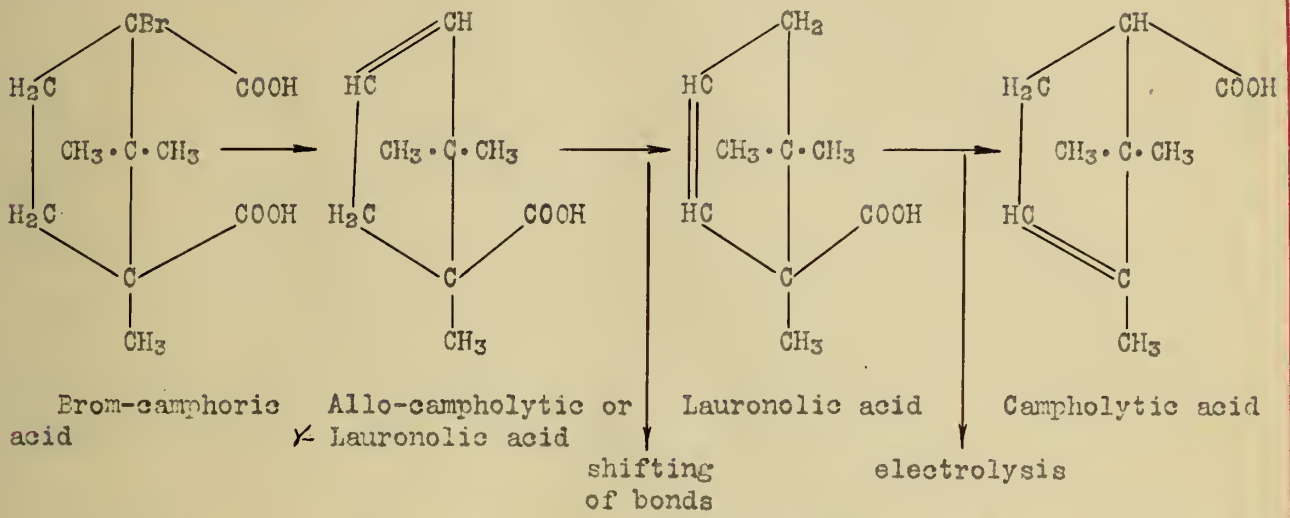
1. Ann. 110, 367.
2. Bull. soc. chim. III, 15, 324.
3. Ann. 289, 5.
4. Ber. 36, 4332 (1903).
5. Ann. chem. Pharm. 187, 156
6. Ber. 25, 923.

Isoamino-camphor was obtained by Tiemann[1] by the treatment of either α- or β-campholenonitrile with concentrated sulphuric or hydriodic acid and also by the action of these reagents on α- or β-campholen-amidic acid. Later[2] he obtained this amino-camphor by treating camphoroxime with concentrated sulphuric acid and also by treating it with hydriodic acid. Isoamino-camphor at its boiling point (254°) transforms itself into campholenic imide. Tiemann in his work deems it essential that the so-called camphor-type be retained in this reaction. Semmler, however, shows[2] that in the formation of the isoamino-camphor from the camphor exime a Beckmann's rearrangement may take place in which case a keto-imide results. This by the addition of water and by a new ring formation may revert to a new bicyclic base. He indicates the following steps:-



1. Ber. 28, 1082, 2168.
2. Ibid. 30, 321.

In the passage from the α- brom-camphoric acid or camphanic acid he obtained the following acid:-

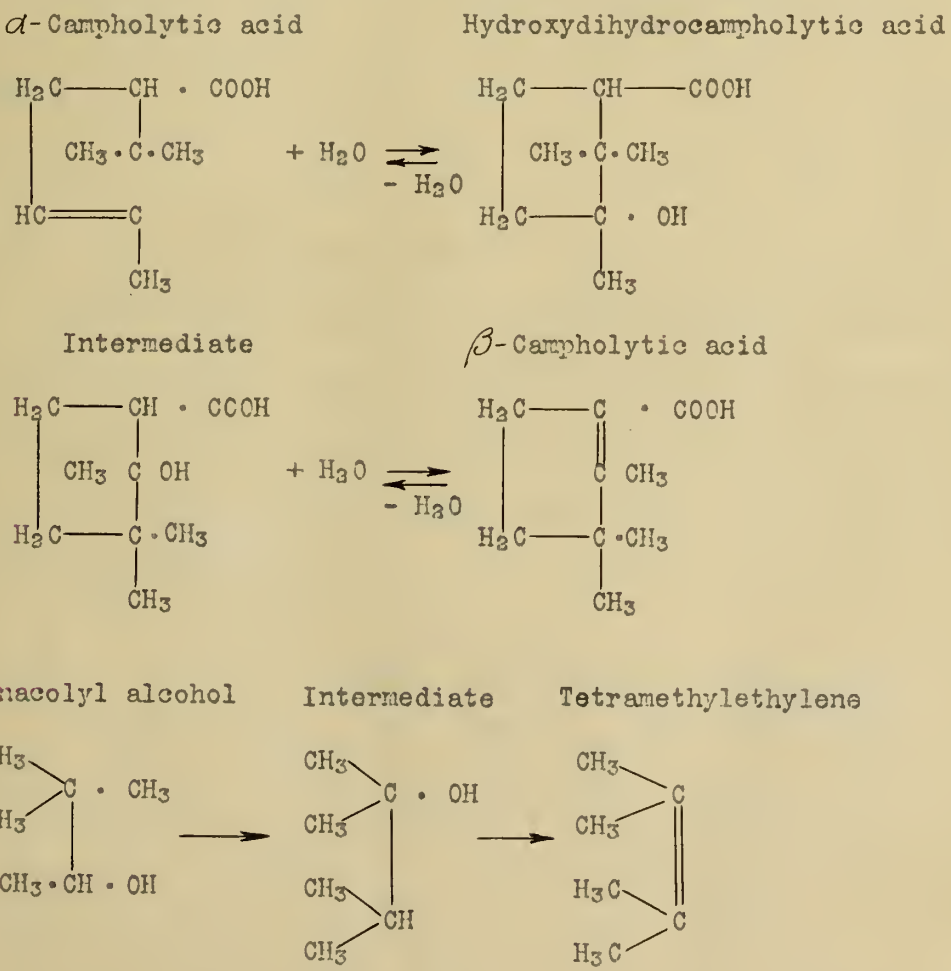


From these by invertion and by new ring closures, or openings, a pinacolin rearrangement can readily occur. The lauronolic acid, in the presence of mineral acids, or by distillation, or gradually even by itself, passes into the isomeric campholactone. β-Campholytic (isolauronolic) acid was first obtained by Walker[1] as a rearrangement product in the electrolysis of the sodium salt of o-ethyl camphorate. It was at that time obtained only as a side-product in the formation of the α -campholytic acid. Noyes[2] obtained it by warming the α -campholytic acid with dilute sulphuric acid and also[3] by allowing it to stand for several days in contact with 50 per cent. sulphuric acid. Noyes[4] also obtained it by treating aminolauronic acid with nitrous acid. The work of Tiemann Kirschbaum and Tigges[5] shows clearly that the α -campholytic acid passes into β -campholytic acid by a peculiar rearrangement. According to them the β -campholytic acid treated with nitric acid went to αα-dimethyl glutaric acid and the α- campholytic went to the αα-dimethyltricarballylic acid. Therefore, in

1. J. Chem. Soc., 63, 498 (1893); 67, 337; 69, 748.
2. Ber. 28, 548
3. Ibid., 28, 553
4. Am. Chem. J., 17, 428
5. Ber. 33, 2935 (1900).

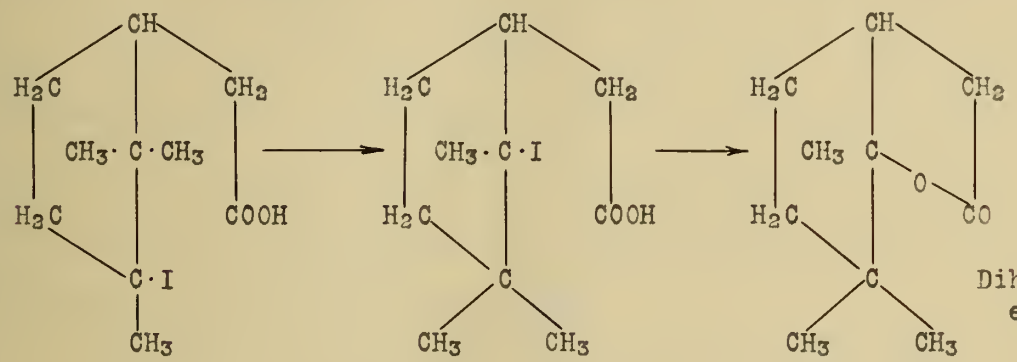
the latter case, passage to the β-campholytic acid would necessitate a wandering of the carboxyl. About the same time Walker and Cormack[1] showed that the reverse, from the β-campholytic acid to the α-campholytic acid, could occur.

These illustrations show that β-campholytic (isolauronolic) acid is formed by a pinacolin rearrangement through the α-campholytic acid, which transformation was first compared with the transformation of pinacolylalcohol into symmetrical tetramethylethylene by Blanc in 1900[2] who took for granted a pinacolin rearrangement in that the hydroxyl can change place with the methyl group. This may be seen more readily from the following:-



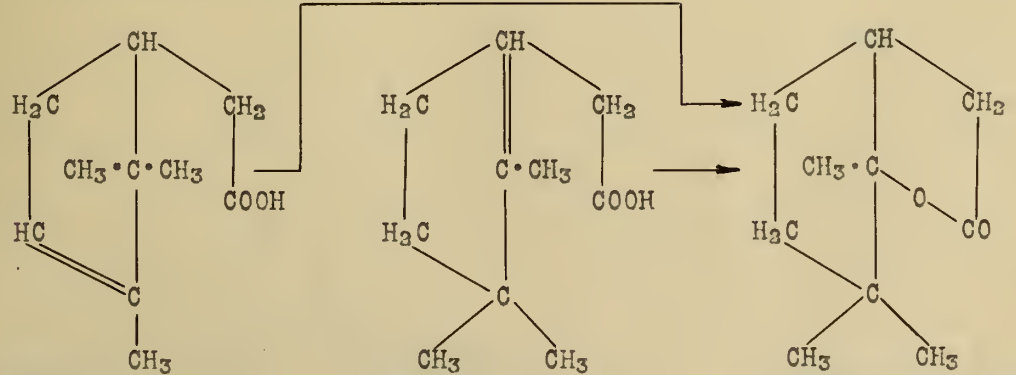
1. J. Chem. Soc., 77, 374 (1900).
2. Chem. Ztg., 24, 1040; Bull. soc. chim. (3) 23, 167 (1900).

By treating the ethyl ester of the amidic acid with nitrous acid the esters of isolauronolic and hydroxylauronolic acids are obtained; another example of the pinacolin rearrangement. The α- campholenicamide hydro-iodide standing in the moist air for several days forms dihydrocampholenolactone. Here the rearrangement must have been caused by the hydriodic acid, the iodine exchanging place with the methyl group. This is again a pinacolin rearrangement:-



Dihydrocampholenolactone

The treatment of the α- campholenic amide with concentrated mineral acid forms the β-amide, which by further action of the concentrated acid eventually goes over into isoamino camphor[1]. Tieman and Mahla[2] obtain the α- dihydrocampholenic acid by saponification of the α- campholenonitrile, which is formed through rearrangement by heating the camphor-imide. Both the α- and β-campholenic acids go to dihydrocampholenolactone.



α- Campholenic acid β-Campholenic acid Dihydrocampholenolactone.

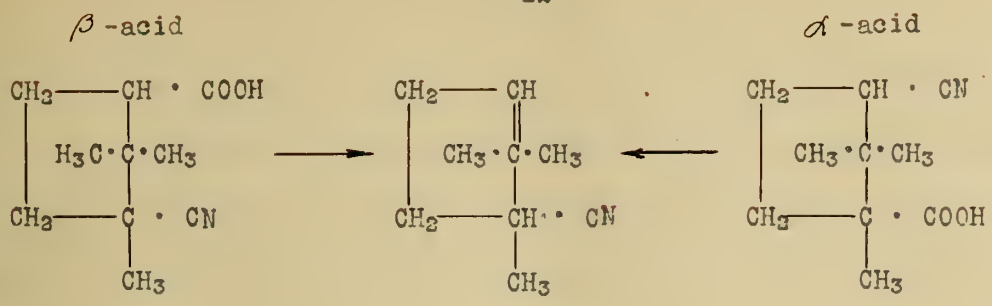
1. Tieniann, Ber. 28, 1083, 2168.
2. Ibid., 33, 1932.

This dihydrocampholenolactone is also formed by treating camphor oxime with dilute sulphuric acid[1]. The camphoroxime in passing over to the α-campholenonitrile undergoes a Beckmann's rearrangement, that is the hydroxyl of the isonitroso group wanders to the tertiary carbon atom which was originally united with a keto group, a splitting of the ring takes place, and, at the same time, the nitrile formation occurs. The passing of the α-campholenic acid to the β- is analogous to the passing of the α-campholytic to the β- acid. This passage from the α- to the β- and β- to the α- might suggest campholenolactone as the intermediary agent. Upon heating, both the α- and β-campholenic acids split off carbon dioxide and yield the same campholene[2]. It must be true that in one of the two a rearrangement takes place within the nucleus by a shifting of the methyl group and the double bond.

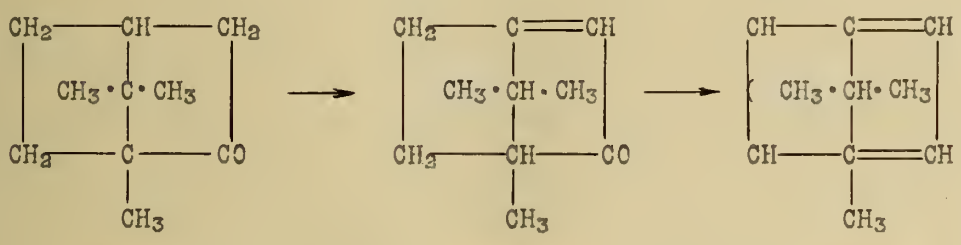
By treating the camphoramidic acids with acetylchloride, Hoogenwerff and Van Dorp[3] obtained two corresponding nitrilic acids, α- and β-camphor nitrilic acids. Tremann, Lemme, and Kerschbaum[4] found that dry distillation of the calcium salts of these two acids produced a splitting of the ring and strangely the same aliphatic nitrile, namely 2,6 dimethyl-5-nitrile, resulted. The β- acid could in this case go to the aliphatic nitrile without a rearrangement, the α- acid, on the other hand, would require a wandering of the nitrile group.

---

1. Tiemann, Ber. 30, 405.
2. Thiel, Ibid., 26, 922 (1893);
   Tiemann, Ibid., 30, 594 (1897);
   Bredt, Ibid., 26, 3055 (1893);
   Bouveault, Bull. soc. chim. 19, 462.
3. Chem. Centr., 155 (1896).
4. Ber. 33, 2953 (1900).



Bredt[1] believes that the α- acid passes intermediately into the imide and this by rearrangement into the β-acid which by further lime distillation yields the dimethylheptene nitrile. An analagous case is that of the camphor into cymene (and carvacrol)[2].



Camphor Carvenone Cymene

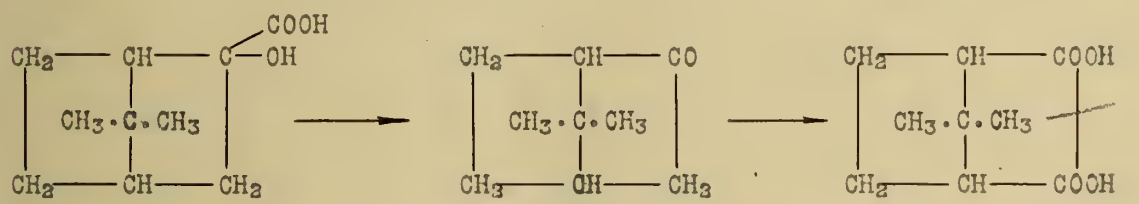
Fenchone.

It is worthy of note that Göttingen, which had furnished the first paper of value on camphor hundred years earlier should in the latter part of the 19th century furnish the first paper on fenchone. R-fenchone was discovered there by Wallach in 1890[3] and the L-fenchone in 1892[4]. It was immediately regarded, on account of its analagous behavior, as a place isomer of camphor[5]. No previously known isomeric compounds of camphor had such characteristics as would enable them to have a structure similar to camphor. However, the reactions

1. Ann. 328, 338 (1903)
2. Ann. chem. Pharm., 314, 369 (1901).
3. Ibid., 259, 324
4. Ibid., 272, 101
5. Ibid., 259, 325; 263, 129.

which obtained in fenchone were parallel with those which obtained in camphor.

The numerous derivatives prepared from the fenchone between 1890 and 1898 aided very little in the determination of the structure of the molecule. However, a study of the oxidation product of fenchene in 1898 threw much light upon the subject; an acid, D-1-hydroxyfenchenic acid, being the result of the oxidiation of D-1-fenchene with permanganate[1]. This hydroxy acid by further oxidation yielded a lower homologue of camphor, fenchocamphorone[2]. Further oxidation of this last product lead to the apo-camphoric acid (camphopyric acid)[3].



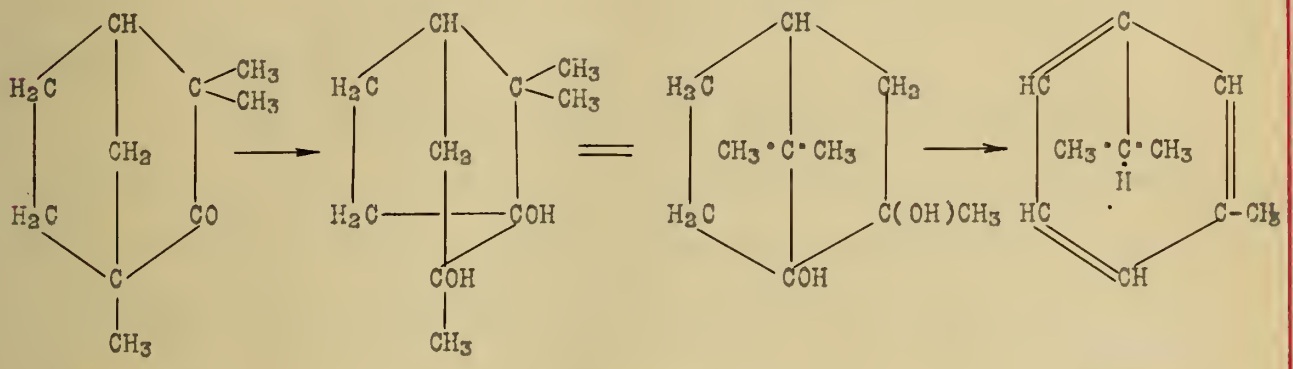
Hydroxyfenchenic acid Fenchocamphorone Apo-camphoric acid

This reaction lead Wallach to set up a formula[4] which was generally accepted, since it explained the rearrangement, under the influence of sulphuric acid, of the apo-camphoric acid into m-cymene and the asymmetric acetylxylene[5]. Wallach's explanation being that the sulphuric acid caused a splitting open of the ring and the withdrawal of water, a rearrangement of the molecule, and an oxidation. According to this the formation of m-cymene into acetylxylene is not surprising Armstrong and Kipping[6] showed that camphor with concentrated sulphuric acid yields the same acetylxylene, and if Bredt's camphor formula is accepted the formation of the acetylxylene can be interpreted in the same way. Both reactions according to Wallach, must be regarded as having intermediate products and ring openings.[7]

---

1. Ann. 302, 382; 362, 184:
2. Ibid., 300, 320.
3. Ibid., 300, 317; 315, 241; 362, 185.
4. Ibid., 300, 319.
5. J. Chem. Soc., 75, 1058; Ann. 315, 296.
6. J. Chem. Soc. 63, 75.
7. Ann. 315, 296.

Semmler in 1905[1] set up a formula by which he attempted to show that the passing over of fenchone into m-cymene was analagous to the transformation of the camphor into the camphene series. He takes two intermediate steps for his formula:-



Fenchone Intermediate m-Cymene

According to this formula fenchone would be brought into close relation to camphenilone and would appear as α- methylated camphenilone.

The close relation between camphor and fenchone derivatives would suggest like structure and similar rearrangements. When fenchone and camphoroxime are treated with acids a nitrile formation takes place, two nitriles being formed in each case. However, Semmler has shown recently that the α- and β- campholenonitriles do not stand in the same relation to each other as the α- and β- fencholenonitriles.

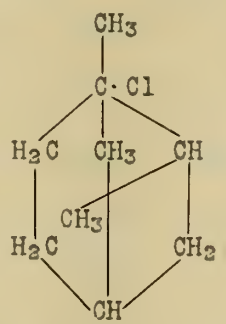
In spite of the similarities between fenchone and camphor, the dissimilarities are of equal importance. All the camphor reactions which involve the neighboring $\underline{CH_2}$ group fall away, as for example, α -halogen, α- nitro, α- amino, etc. Fenchone forms a hydroxycarboxylic acid in which the carboxyl and hydroxyl are bound to the same carbon atom. This is not true of camphor. Semmler[2] deems it inessential to have a pinacolin rearrangement in the fencho-

1. Chem. Ztg., 29, Nr. 103; Die Aetherischen Oele, Band III, 576.
2. Die Aetherischen Oele, Band III, 559.

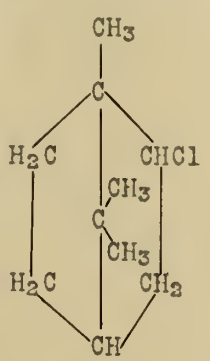
lenic acid; whereas in the passing of the α- into the β-campholenic acid such a rearrangement must be taken into consideration.

It would hardly be possible to take up a discussion of the camphor-camphene and fenchone -fenchene molecules without taking into consideration pinene, which has played such a large part in the clearing up of the rearrangements in these series.

In 1887[1] it was first taken for granted that in addition to the ethylene bond there was another weak or easily broken union in the pinene molecule. At that time Wagner's formula was the more acceptable and the addition of dry hydrochloric acid to the molecule was given the formula:-



To get to the artifical camphor by the splitting off of the HCl from this molecule an atomic rearrangement is necessary. Wagner and Brickner in their work regarded that product as already a bornylchloride and therefore that the rearrangement of the molecule immediately followed the addition of hydrochloric acid to the pinene. Their formula was as follows:-



1. Ann. 239, 5.

The formula most generally accepted at present was set up by Wallach in 1907 when he showed that the pinene hydrochloride of the first structure really had properties entirely different from the one leading to artificial camphor.

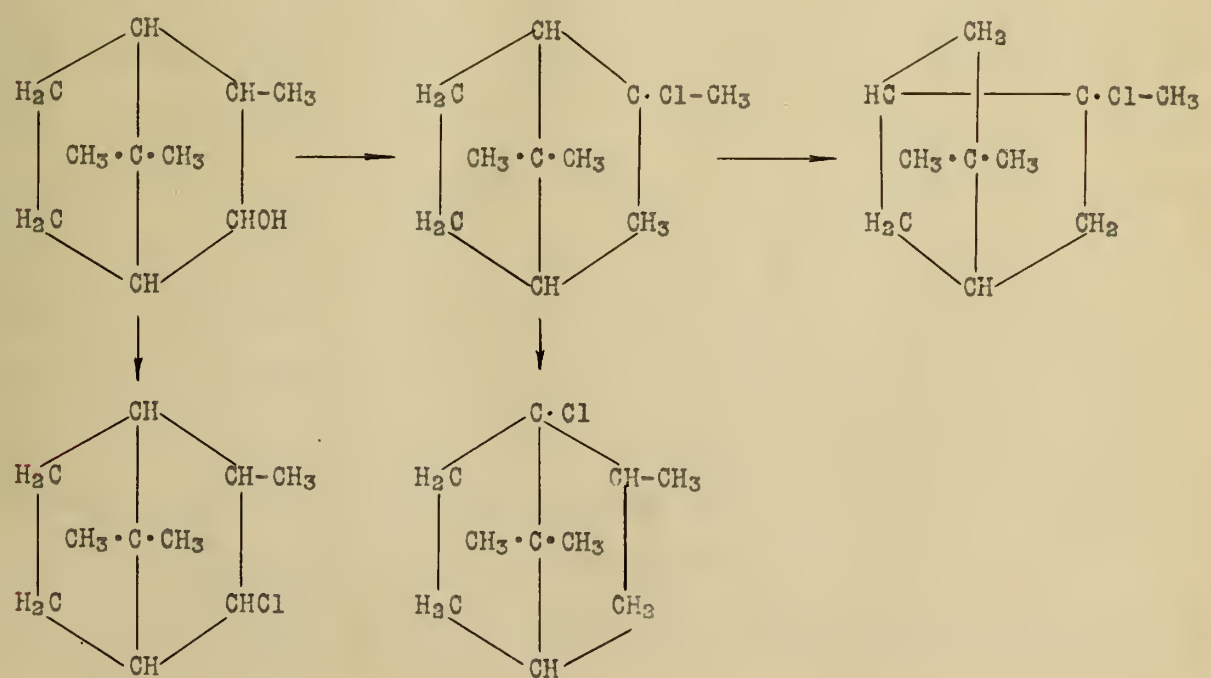
The properties of pinene and its derivatives are very closely related to those of the camphene and fenchene as can be seen from the following in which the rearrangements also become apparent.

Camphene[1] like pinene takes up one molecule of hydrochloric acid and in general the camphene hydrochloride resembles the pinene hydrochloride[2]. The two, however, differ in the manner in which they hold the HCl. In camphene hydrochloride the HCl is easily split off again and camphene regenerated. Pinene hydrochloride, on the other hand, splits off HCl with difficulty and no pinene is formed but camphene.[3] This difference in behavior leads to the suspicion that in camphene hydrochloride the splitting off of the HCl is caused by the chlorine and the hydrogen being in ortho position to each other, whereas in the pinene hydrochloride the splitting off occurs with atoms further apart. Fenchene with one molecule of hydrochloric acid yields fenchene hydrochloride[4]. Wallach obtained two chlorides and by splitting off HCl procured two different fenchenes, a right and a left, the one corresponding to the 137° melting hydroxyfenchenic acid, the other to the 152° melting acid[5]. Bornyl chloride only gave one camphene. This made Wallach's formula for fenchene[6] seem doubtful and lead to the presupposition of a rearrangement from the fenchyl alcohol to fenchene. Wallach little suspected this in 1891[7] when he prepared it analagously

---

1. Ann. chem. Pharm. 252, 140.
2. Ibid., 230, 231 and 233; 245, 209.
3. Ibid., 239, 6, 7.
4. Ann. 302, 382 (1898)
5. Ibid., 284, 333; 302, 371.
6. Ibid., 300, 320 (1898).
7. Ibid., 230, 150.

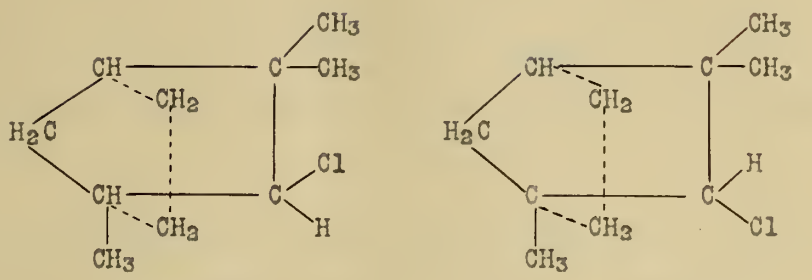
to the camphene out of borneol through the bornyl chloride. He explains his formula in 1898 by considering that the hydrocarbon resulting from the D-l-fenchyl alcohol, that is, the first formed fenchene, undergoes a shifting of bonds. This shifting of bonds is frequently the case in the terpene hydrocarbons and therefore might be expected in the passing from fenchyl alcohol ⟶ fenchyl chloride ⟶ fenchene. If phosphorus pentachloride instead of hydrochloric acid is allowed to act on borneol a bornyl chloride is obtained which no longer corresponds to borneol but to a different alcohol, isoborneol, which is identical with the camphene hydrochloride. This might be called a rearrangement from the camphor to the camphene type. The true borneol chloride is the pinene hydrochloride. The case of the secondary fenchyl alcohol, which with phosphorous pentachloride gives rise to fenchyl chloride is analagous[1]. Kondakow states that this fenchyl chloride is principally a tertiary chloride and considers the following rearrangement:-



secondary fenchyl chloride tertiary fenchyl chloride

1. J. pr. Chem. II, 62, 1.

Semmler[1] suggests for the chlorides the following structures:-



I II

According to him I would correspond to the fenchyl alcohol (m. p. 45°) and would be analagous to the true bornyl chloride, the pinenehydrochloride. The fenchyl chloride II then corresponds to the isobornyl chloride provided this is regarded as a secondary stereoisomer of the pinene chlorhydrate. The phosphorus pentachloride on the fenchyl alcohol (45°) yields both chlorides and even more of II than I. The explanation offered for this behavior is very logical and is as follows, fenchyl chloride II splits off the hydrochloric acid very readily and passes into fenchene which gives the hydroxyfenchenic acid melting at 159°. It can be considered that at higher temperatures the following rearrangements take place. The hydrochloric acid adds itself to the two terpenes, and we have two tertiary chlorides. These chlorides rearrange into the secondary fenchyl chloride similar to the rearrangement of the camphene hydrochloride into the secondary isobornyl chloride. This would be in accordance with II. That the rearranging factor is temperature is in accord with experience[2]. Allowing phosphorus pentachloride to act in the cold upon fenchyl alcohol a splitting off of HCl forms fenchene I. If on the other hand, the temperature is allowed to rise during the experiment the main product is fenchene II.

It is evident that rearrangements of the above type would be more apt

---

1. Die aetherischen Oele, Band III, 547.
2. Author, 1908, Göttingen.

to occur in the fenchene than in the camphene series, since in the fenchene series the labile hydrogen is in the ring where it is easily splt off. This is not true of camphene. It is also evident that a methyl group can easily wander from the dimethylated carbon atom, thereby giving rise to new fenchylchlorides and fenchenes.

Wallach's late synthesis[1] of the β- pinene and the two fenchenes shows the ease with which rearrangements may take place in these series. Both fenchenes and the β-pinene arise when nopinole acetic acid is treated with a dehydrating agent and then carbon dioxide split off.

Gardner and Cockburn[2] by oxidation of the crude fenchene obtained apocamphoric acid (camphopyric acid), which had already been obtained by Wallach through the D-d-fenchocamphorone[3]. This oxidation of the fenchenes goes to prove that they belong to the "pentocean" system, but differ from the camphor and camphene in that the methyl groups occupy a different position. The relation of the borneol and isoborneol to the camphor can be seen by the difficulty with which camphene is formed when water is split out of borneol. If the borneol is treated with phosphorus pentachloride a camphene hydrochloride (isobornyl chloride) is formed. In both cases there is a transition from the camphor to the camphene type. This rearrangement can be explained by a peculiar configuration of the "pentocean" system. A five ring in this system is easily split open and a different five ring is formed with equal ease. It is to this peculiarity that the numerous rearrangements in both of these systems can be attributed.

---

1. Terpene and Campher - Wallach, 259.
2. Proc. Chem. Soc., No. 187, 8 (1897).
3. Ann. 300, 317; 315, 291.

Parallelisms in the Camphor and Fenchone Series

Fenchene Chloride ⟶ Fenchene (Ann. 263, 149; 302, 372)

Bornyl Chloride ⟶ Camphene (Ann. 230, 233: Ber. 25, 917)

Hydroxyfenchenic Acid ⟶ Fenchocamphorone (Ann. 300, 314)

Hydroxycamphenilic Acid ⟶ Camphor (Ann. 353, 225)

Camphoroxime ⟶ Campholenonitrile (Ber. 20, 484: Ber. 20, 110)

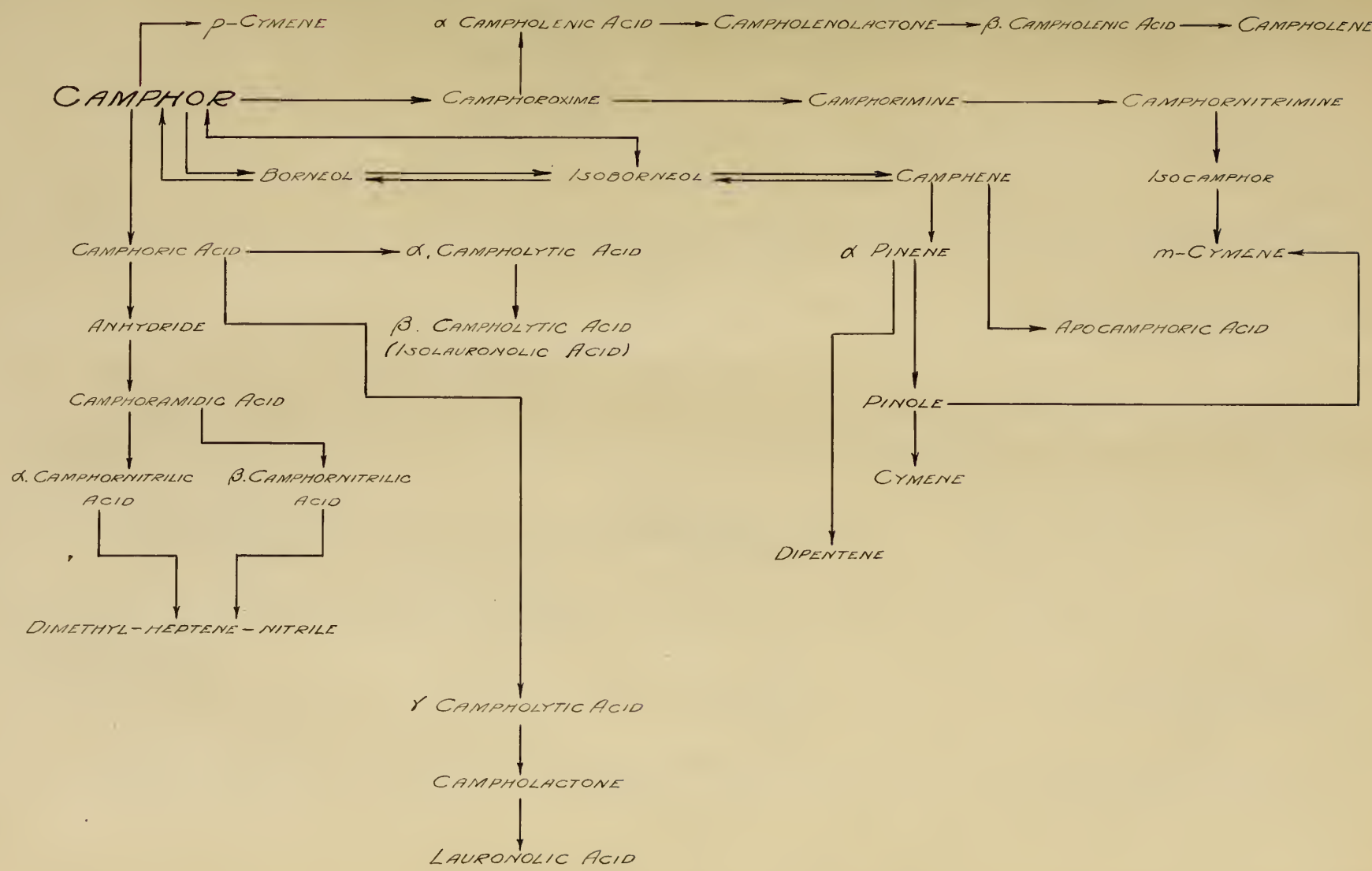
Fenchonoxime ⟶ Fencholenonitrile (Ann. 259, 328)

Fenchocamphonoxime ⟶ Fenchocamphonitrile (Ann. 300, 316)

Pinocamphonoxime ⟶ Pinocamphonitrile (Ann. 300, 28)

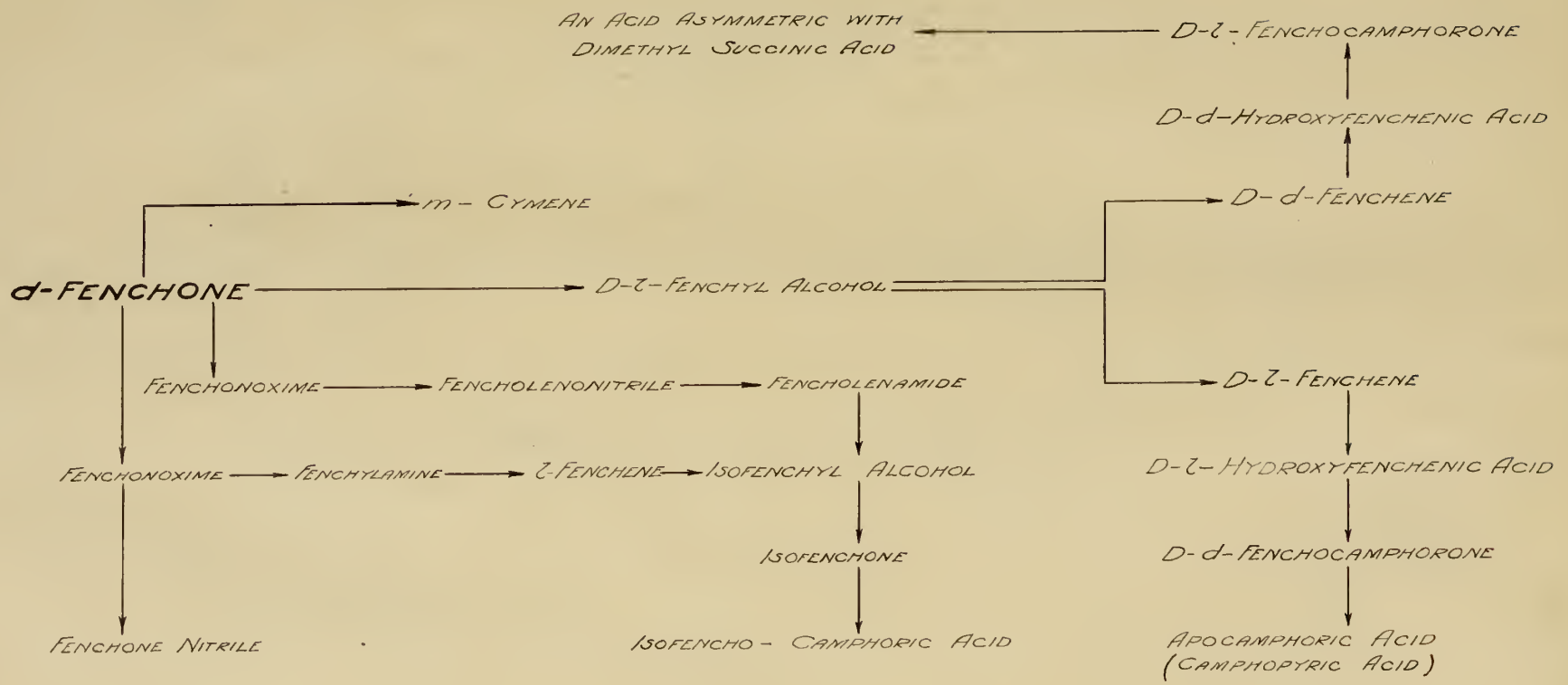
REARRANGEMENTS —— CAMPHOR

PLATE I



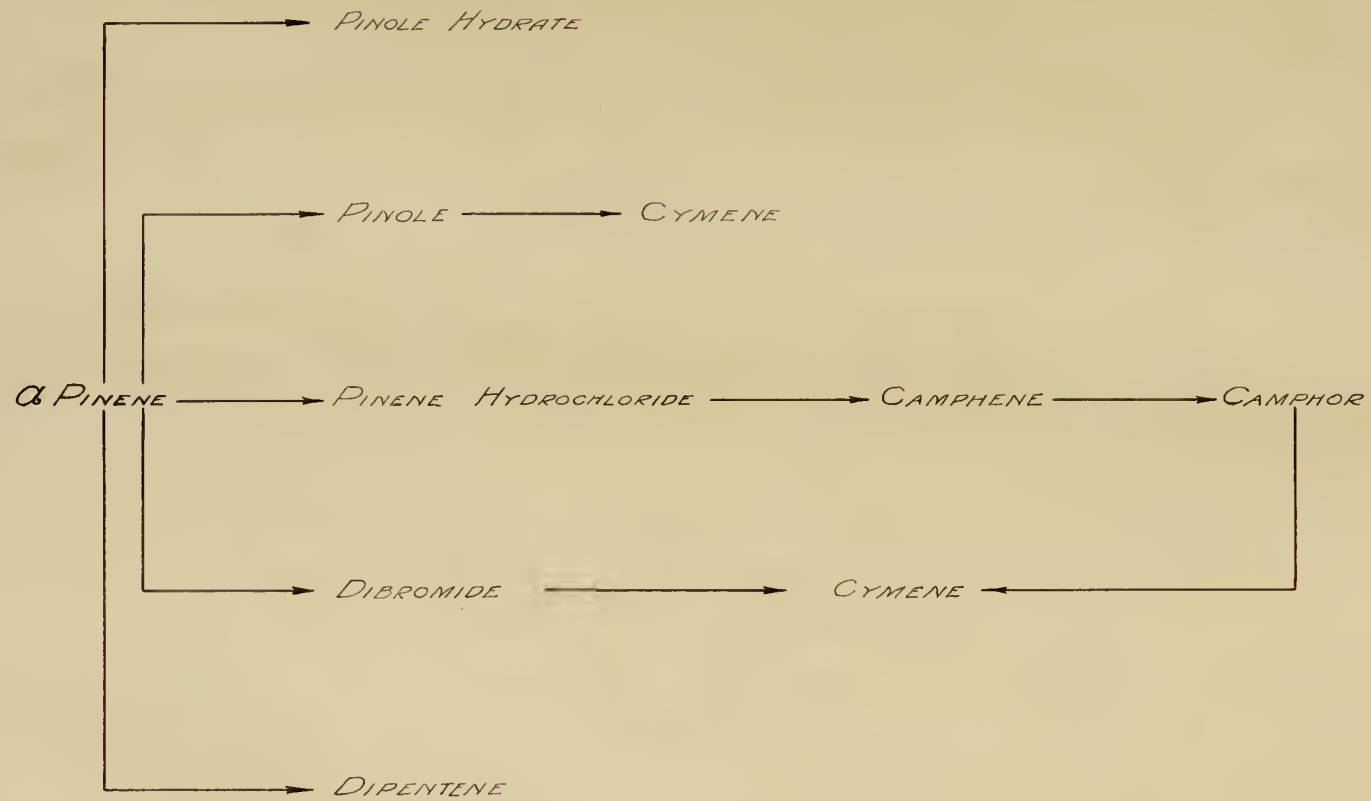
REARRANGEMENTS —— FENCHONE

PLATE II



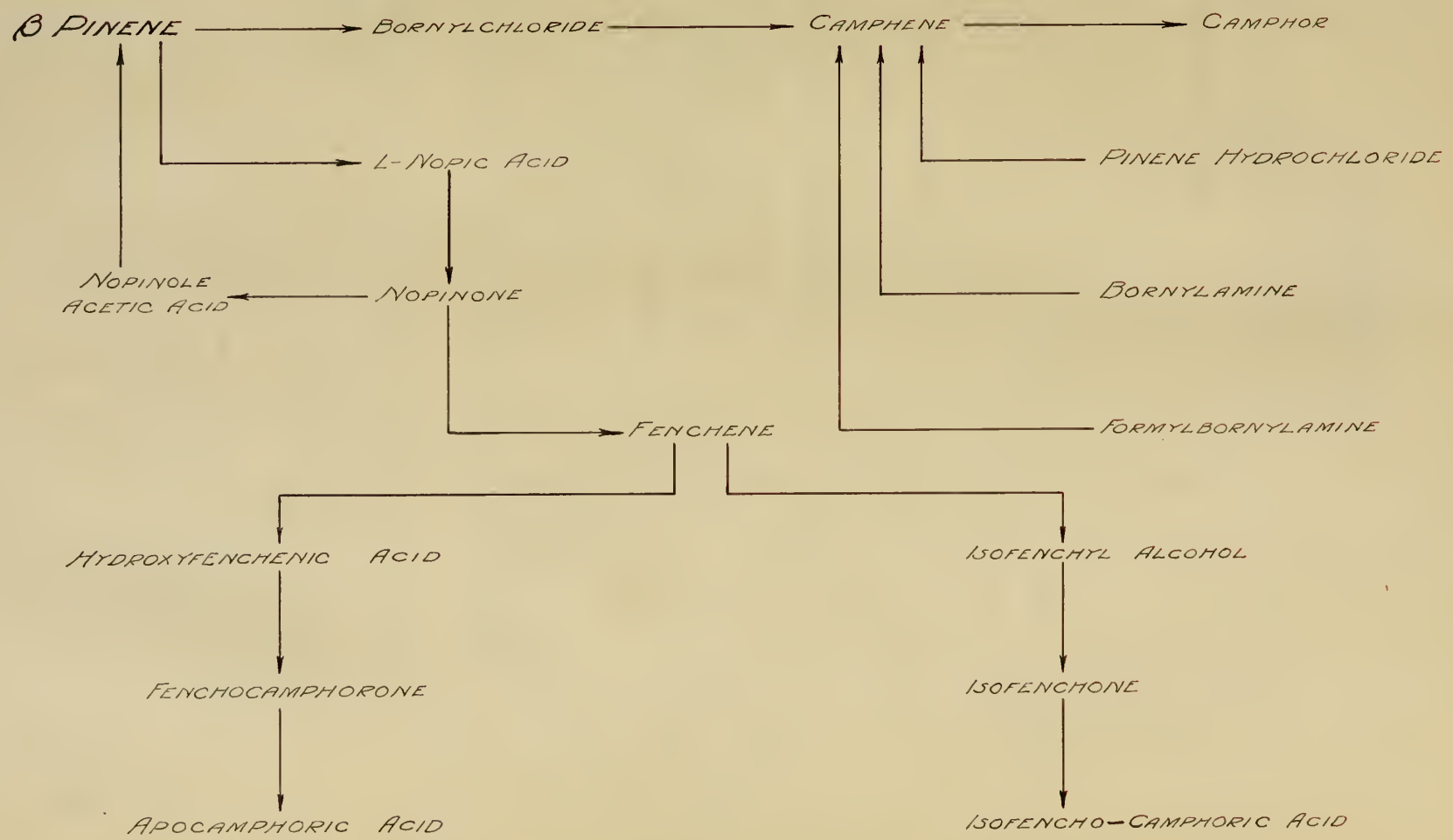
REARRANGEMENTS —————— PINENE

PLATE III



REARRANGEMENTS —— PINENE

PLATE IV



Experimental Part.

Camphoric acid and the anhydride were prepared according to Noyes[1].

Camphoramidic acid:- The method of Noyes and Taveau[2] was followed with one exception. The flask was shaken until the maximum temperature was apparently reached, it was then opened and dry gaseous ammonia lead into the mixture for five minutes. The flask was closed again and shaken vigorously until the mixture began to cool. After this it was rapidly cooled by crushed ice. The ammonium salt which separated was filtered on a plate and sucked dry. The yield by this method was about eight per cent higher than in Taveau's method.

Hydrochloride of Aminolauronic acid was prepared according to Noyes[3]. In the purification some variations were made. The crude product was dried and powdered and a fairly saturated solution prepared with cold water. This was filtered and 15 per cent. of concentrated hydrochloric acid added. This solution was seeded with some pure hydrochloride and stirred to start crystallization. It was allowed to stand three hours, then filtered and sucked dry. A nice clean product melting at 303° was obtained in this manner.

Preparation of the ethyl ester of amino-lauronic acid from the amino-lauronic acid hydrochloride.

Considerable experience was obtained in the preparation of the ethyl ester of aminolauronic acid. The most satisfactory method was finally found to be the heating of 20 grams aminolauronic acid hydrochloride, 6 cc. of concentrated sulphuric acid and 80 cc. of absolute alcohol on a water bath in a stout bottle connected with an upright condenser, the top of which was connected with a glass tube dipping under a column of 50 cm. of mercury. After heating for 48

---

1. Am..Chem. J., 16, 505.
2. Ibid., 32, No. 3, 287.
3. Ibid., 16 506.

hours the alcohol was distilled off under diminished pressure, and then 50 cc. of water and a slight excess of sodium hydroxide (3 cc. = 1 g) added, the solution being cooled, thoroughly during the neutralization. The ester was then taken up with ether. The yield was 35 per cent. Yields from 50 to 65 per cent were obtained with pressure bottles. The objection to this method was that it was almost impossible to find any glass which would resist the pressures developed from the ethyl chloride formed. Magnesium citrate bottles served the purpose fairly well, although they too frequently exploded.

The alkaline liquid from which the ester had been extracted was made strongly acid with concentrated hydrochloric acid, thereby recovering the amino-acid.

Decomposition of the ethyl ester of amino-lauronic acid.

Formation of hydroxylauronic ester, $C_8H_{14}(OH)CO_2C_2H_5$ and

lauronolic ester, $C_8H_{13}CO_2C_2H_5$.

The golden colored and sweet smelling ester was treated with a little less than the calculated amount of sulphuric acid (25 per cent.). This is best accomplished by using tumeric paper and adding the sulphuric acid cautiously until the tumeric shows faint signs of blue. The solution was then cooled and the calculated amount of sodium nitrite (1 : 5) carefully added with cooling. It was allowed to stand until all action ceased which required from two to six hours. The oily layer formed was then taken up with ether and the ethereal solution washed with a very dilute solution of sodium carbonate and with water, dried with anhydrous sodium sulphate, and distilled under diminished pressure. The weight of the mixed esters obtained was only one-half of the aminolauronic ester. The mixed esters were put into a Claisen bulb, and fractionated under diminished pressure. The portion distilling over between 110°- 115° at 25 mm.

decolorizes potassium permanganate while that distilling over at 150° at 30 mm. does not effect it.

Rotation of distillate coming over at 110° - 115° and 25 mm. pressure.

α -lauronolic ester, $C_8H_{13}CO_2C_2H_5$

$$[\alpha]_D^{26.0} = 56.61 \qquad d_4^{20} \; 0.9514$$

Rotation of distillate coming over at 150° and 30 mm. pressure.

Hydroxylauronic ester, $C_8H_{14}(OH)CO_2C_2H_5$

$$[\alpha]_D^{33.5} = 6.73 \qquad d_4^{15} \; 1.0099$$

Analysis of 150° product

0.2036 gram substance gave 0.5551 gram CO_2, 0.2036 gram H_2O

or 66.08 per cent. C, 9.96 per cent. H

0.2145 gram substance gave 0.5180 gram CO_2, 0.1873 gram H_2O

or 65.86 per cent. C, 9.78 per cent. H

Calculated for $C_8H_{14}\begin{cases} CO_2C_2H_5 \\ OH \end{cases}$ C = 65.94, H = 10.06.

Copper salt of the hydroxy acid $(C_8H_{14}\begin{cases} CO_2 \\ OH \end{cases})_2Cu + H_2O$.

The salt was prepared by treating the hydroxylauronic ester, C_8H_{14} $C8H_{14}(OH)CO_2C_2H_5$) with 2 1/2 times the theoretical amount of alcoholic potash. This is boiled on the water-bath in a flask with an upright condenser for four hours, the alcohol evaporated off, and hydrochloric acid slowly added in order to get the free hydroxy acid. This acid is extracted with ether. The ether is

evaporated off and water added. To this solution about 1 1/2 times the theoretical amount of calcium carbonate is added. The calcium salt formed is filtered off and converted into the copper salt by dissolving it in H_2O and adding a ten per cent. solution of cupric chloride. The salt formed is magnetic and nearly insoluble in water.

I 0.09446 gram copper salt gave 0.01775 gram CuO or 15.01 per cent. Cu

II 0.1206 gram copper salt gave 0.02245 gram CuO or 14.88 per cent. Cu

The water seems to be fixed very firmly in the molecule. Not until the salt was heated for 8 hours between 150° - 160° did the weight become constant.

0.0918 gram lost 0.0079 gram or 8.60 per cent. at that temperature.

Calculated for $(C_8H_{14}(OH)CO_2)_2Cu + 2H_2O$, Cu 15.01 per cent., H_2O 8.55 per cent.

Ketone reaction.

0.4 gram of the ester $(C_8H_{14}(OH)CO_2C_2H_5$ was treated with the theoretical amount of Beckmann's mixture, heated and shaken for one-half hour, then allowed to stand 12 hours. A layer was formed which was taken up with ether. This ethereal solution gave a distinct test for a ketone with phenyl hydrazine. The experiment was so carried out that the amount of carbon dioxide evolved could be determined. The carbon dioxide corresponded to 14 per cent. of the acid used. Not enough of the ketone was obtained for identification.

Oxidation of the hydroxy acid, $C_8H_{14}\begin{matrix}COOH\\OH\end{matrix}$.

0.4 gram of hydroxy acid was digested on the water bath with concentrated nitric acid for two days in a 50 cc. flask sealed to an upright condenser. The nitric acid was then evaporated off and water added and boiled off

several times. The residue was finally taken up in water and made distinctly alkaline with ammonium hydroxide. It was then cooled and mixed with a strong solution of barium chloride. This was warmed for 30 minutes, then filtered from any precipitate that had formed. The filtrate was heated on the water bath to boiling, which caused the camphoronic acid to precipitate as a sparingly soluble barium salt. It was then filtered, washed, and dried. The barium salt was then suspended in water and the theoretical amount of sulphuric acid (1-3) necessary to liberate the camphoronic acid, added. The mixture was warmed, the barium sulphate filtered off and the filtrate concentrated and allowed to stand twenty-four hours. A crystalline body formed, with a melting-point of 134°. The crystals conformed to the anhydride of camphoronic acid. An equivalent amount of known barium camphoronate was treated in a similar manner and a product melting between 132 - 134° was obtained. Mixing the two products did not change the melting point. It seems utterly impossible to get camphoronic acid from small quantities of barium camphoronate by means of the sulphuric acid. Apparently the acid goes to the anhydride.

Again 1.31 grams of the hydroxy acid ($C_8H_{14}(OH)COOH$) were treated in a similar flask with 15 cc. of nitric acid (1.2 sp. gr.) and digested for 12 hours. The product upon cooling crystallized from the liquid in needles having a fibrous, silky, and radiating structure. When recrystallized from ligroin it melted between 171 - 172°. The melting point was not changed by recrystallization. The body is rather volatile, soluble in ligroin, readily soluble in ether and alcohol, and is insoluble in cold sodium carbonate. On account of the limited quantity of the substance only one analysis could be made.

0.177 gram substance gave 0.368 gram CO_2, 0.163 gram H_2O

or 56.7 per cent. C, 10.35 per cent. H.

Although no analysis was made for nitrogen, it probably was a nitroderivative

of the hydroxy acid. The formula to which it most closely corresponded to was $C_9H_{20}NO_3$ where C = 56.8 per cent. H = 10.53 per cent.

The mother liquor from the above crystals was evaporated to dryness, water added and evaporated. This was repeated several times. The gummy residuewas finally taken up with warm water and neutralized with a hot solution of barium hydroxide. A heavy sandy precipitate came down. This was filtered, dried, finely pulverized and warmed for about two hours with nitric acid, (1.4 sp.gr.), enough nitric acid being taken to convert it into a thin paste. It was then filtered off on a hard filter. The solution was evaporated to dryness repeatedly with water and the residue finally recrystallized from hot water. A product was obtained which melted at 156°. This is the method as given by Bredt for the preparation of the camphoronic acid[1]. It seems impossible to get free camphoronic acid in small quantities by means of the Perkin and Thorpe method[2] the anhydride of the acid always forming. The melting-point of the above product would agree with Perkin's d-camphoronic acid which melts at 156°. The product was then treated with a little acetyl chloride and warmed until all the salt was in solution. Then the acetyl chloride was evaporated off. The residue was extracted with hot ligroin and from this solution, after evaporation, a compound was obtained which melted between 135 - 136°. This agrees with camphoronic anhydride. Mixing this product with the known anhydride did not change the melting-point.

Liberation of amino-lauronic acid from its hydrochloride; convertion of the acid into the anhydride; preparation of the nitroso derivative of the anhydride of amino-lauronic acid.

The aminolauronic acid hydrochloride was taken in lots of 100 grams each and made into a thick paste with water, which took about 100 cc. of water.

1. Ann. 292, 75 (1896).
2. J. Chem. Soc., 71, 1190 (1897).

To this semi-thick mass was added 60 cc. of sodium hydroxide (3 cc. = 1 gram). The mixture was digested on the water bath for about 30 minutes, then cooled, filtered and dried. The free acid obtained in this way was placed in a retort and heated in a metal bath up to 290°, at which temperature a very little of the anhydride distilled over, the main bulk remaining in the retort. The yield of the anhydride was about 77 per cent. of the weight of the acid. The anhydride was used directly for the preparation of the nitroso compound. In the preparation of the nitroso derivative 36 grams of the anhydride were dissolved in 30 cc. of concentrated hydrochloric acid and 18 grams of sodium nitrite slowly added. A lemon-yellow precipitate formed. This was filtered off and sucked dry. The melting-point of the uncrystallised product was 136°, when recrystallised once from alcohol it was 138 - 139°.

Preparation of the isocampholactone from the nitroso compound.

10 grams of the nitroso compound were placed in a roomy flask. To this 30 cc. of aqueous 10 per cent. sodium hydroxide solution was added and the flask closed with a stopper which had two glass tubes running through it, one extending under the liquid in the flask and through which a lively stream of steam was passed, the other leading into a condenser which carried off the hydrocarbon as it was being formed. The contents in the flask were gently boiled over a free flame until the decomposition was complete. Then 10 grams of the nitroso compound were again added together with 30 cc. of the 10 per cent. sodium hydroxide solution, and the process repeated as before. This repetition was continued up to 50 grams, then the apparatus was disconnected, cooled and the theoretical amount of 1 : 1 sulphuric acid added. The acidified liquid was then extracted five times with ether, the ether evaporated off and the residue shaken with a strong potassium carbonate solution. After the separation of the carbon-

ate solution the remaining liquid was again extracted repeatedly with ether. The ethereal solution was dried with sodium sulphate and the ether evaporated off. The residue was distilled under diminished pressure and the isocampholactone distilled over at 119° at 20 mm. pressure.

The yield of hydrocarbon from 122 grams of the nitroso compound was 32 grams, isocampholactone 26.5 grams.

Rotation of the isocampholactone $[\alpha]_D = -63.1^\circ$ at 28°

Action of ammonium hydroxide on isocampholactone.

0.5 gram isocampholactone was placed in a tube with 20 cc. of strong ammonium hydroxide. The tube was sealed and heated until all the isocampholactone was in solution. This took about 18 hours. It was then opened and no pressure could be detected. The solution was poured into a crystallizing dish and allowed to evaporate in a vacuum desiccator over sulphuric acid. The resulting residue melted at 135°. The product was insoluble in ligroin, dissolved readily in absolute alcohol and by the addition of a few drops of ligroin to the alcoholic solution a beautiful crystallized product formed, which melted at 137°. The yield was 0.1 gram from 0.5 gram. Some of the isocampholactone was recovered unchanged by simply cooling the ammoniacal solution thoroughly after it had been heated for 18 hours. In the air or upon heating, the product went back to the isocampholactone. It also partly volatilized in the air. To get the product pure the residue, after evaporation of the liquid, was pressed on a porous plate that had been warmed between 40° and 50°. This took up the unchanged isocampholactone that remained. It was then washed several times on the plate with ligroin and was ready for analysis.

Calculated for C_8H_{14}(COONH$_4$)(OH) :- C = 57.14; H = 10.05; N = 7.4 per cent.

0.0747 gram substance gave 0.1568 gram CO_2; 0.0685 gram H_2O

0.348 gram gave 22.0 cc. of N at 22° and 744 mm. present. Found C = 57.2; H = 10.2; N = 7.26 per cent.

The amide was not formed but the ammonium salt of the hydroxy acid. It might, of course, be that the amide was an intermediate product in this case.

Oxidation of the isocampholactone.

Three grams of isocampholcatone were heated 72 hours with nitric acid (1.27 sp. gr.) in a 50 cc. flask sealed to an upright condenser. The heating was continued till the oily layer of lactone disappeared, a little concentrated acid being added from time to time. A beautiful product, which partly sublimed into the condenser during the oxidation, separated into crystalline form on cooling the solution. It was quite volatile and crystallized from ligroin in needles. It melted sharply at 122° and boiled at 272°. The recrystallized product was analyzed. The following analyses represent four different preparations.

I	0.1448	gram	substance	gave	0.2978	gram	CO_2	and	0.0929	gram H_2O
II	0.1115	"	"	"	0.2280	"	"	"	_____	" "
III	0.1137	"	"	"	0.2287	"	"	"	0.0736	" "
IV	0.1055	"	"	"	0.2120	"	"	"	0.0671	" "
V	0.1004	"	"	"	0.2018	"	"	"	0.0649	" "
VI	0.1062	"	"	"	0.2140	"	"	"	0.0680	" "
VII	0.1151	"	"	"	0.2317	"	"	"	0.0709	" "

Calculated for $C_9H_{13}O_2 \cdot NO_2$		Found						
		I	II	III	IV	V	VI	VII
C	54.29	56.09	55.89	54.85	54.8	54.81	54.9	54.90
H	6.53	7.19		7.25	7.12	7.24	7.12	6.95
N	7.04						7.1	7.2

Rotation $[\alpha]_D = -85.4$ at 40°

A part of the analyses were not very satisfactory. It is interesting to note that Schryver's carbon results on the nitrocampholactone ran about the same as those obtained in this case, namely 54.79 per cent.

Phosphorus trichloride and penta-chloride have no effect on the oxidation product.

0.5 gram of the oxidation product was treated with 1 gram of phosphorus trichloride and heated for 15 minutes. The liquid mass was allowed to cool. Even after standing 24 hours no crystals appeared; it was then poured into ammonium hydroxide which was being cooled with an ice mixture. A precipitate formed at once and without recrystallizing melted at 119°. Recrystallized from ligroin the melting-point was again 122°.

0.5 gram being treated with twice its weight of phosphorus pentachloride, there was no action in the cold, on warming on the water-bath, however, a yellowish liquid formed but no hydrochloric acid gas was evolved. After allowing the liquid to cool a crystalline mass separated; on recrystallizing from ligroin it melted at 120°. Further recrystallization showed it was the original substance.

Acetic anhydride or acetyl chloride have no action on the nitro compound.

An attempt was made to oxidize the isocampholactone with Beckmann's mixture. However, after heating the isocampholactone with the mixture for

twenty-four hours on the water-bath all of the isocampholactone was extracted unchanged from the solution with ether.

The action of potassium permanganate was also tried on the isocampholactone but without effect.

Reduction of the nitro-isocampholactone with tin and hydrochloric acid. Formation of amino isocampholactone.

1 gram of the nitro-isocampholactone was suspended in 5 times its weight of concentrated hydrochloric acid. While this was being cooled by ice water, granulated tin was gradually added until no more heat seemed to be evolved. Concentrated hydrochloric acid was then added in three portions of one gram each and granulated tin until all the nitro compound had gone into solution. This was then filtered off from the tin and was perfectly colorless. It was made alkaline with sodium hydroxide (3 cc. = 1 g), care being taken not to have a large excess of the sodium hydroxide, otherwise the reduction product seemed to decompose. A large excess of sodium hydroxide, added to the acid solution yielded a product which melted at 152°; the yield from 1 gram being 0.1 gram. When the solution was made only slightly alkaline a product resulted upon extraction with ether which melted at 84°. The yield from 1 gram gave 0.35 gram of the reduction product. When dissolved in absolute ether and treated with dry hydrochloric acid a white precipitate, readily soluble in water, was obtained. It was probably the hydrochloride.

This hydrochloride dissolved in water upon being treated with platinum tetrachloride and allowed to stand for some time gave a yellow crystalline body.

Analysis of 152° product.

0.1037 gram substance gave 0.2253 gram CO_2; 0.0791 gram H_2O

0.1051 gram substance gave 0.2289 gram CO_2; 0.0809 gram H_2O.

Found C = 59.25 per cent., H = 8.55 per cent., N = 7.09 per cent.

C = 59.39 per cent., H = 8.62 per cent.

Calculated for $C_9H_{13}O_2NHOH$, C = 58.47, H = 8.40, N = 7.45 per cent.

Analysis of 84° product

Found

0.1062 gram substance gave 0.2462 gram CO_2, 0.0904 gram H_2O

0.1020 gram substance gave 0.2360 gram CO_2, 0.0876 gram H_2O

Calculated $C_9H_{13}C_2NH_3$, C = 63.90, H = 8.87, N = 8.28 per cent.

Found C = 63.22 per cent., H = 9.54 per cent., N = 8.10 per cent.

C = 63.10

There can be no doubt that the 84° melting product was the amino derivative of the nitro-isocampholactone.

Reduction of the nitro-isocampholactone with zinc dust and glacial acetic acid. Formation of a hydroxylamino-lactone.

1 gram of the nitro-compound was dissolved in about eight times its weight of glacial acetic acid and zinc dust added in small quantities, great care being taken to keep the solution cold. Zinc dust was added until further addition of it caused no appreciable rise in temperature. The solution was then filtered from the excess of zinc dust and zinc acetate, the residue washed with as little water as possible. This was then made alkaline with sodium hydroxide, the temperature being kept low by cooling with ice. Precautions must be taken not to use too large an excess of the sodium hydroxide. The best results were obtained by adding about 5 per cent. more than is required to neutralize the acid solution. The alkaline and turbid solution was then extracted with ether and the ethereal solution dried with anhydrous sodium sulphate. The dried solu-

tion was allowed to evaporate off and a crystalline body remained which melted at 142°. When recrystallized from dry ether the product melted at 144°. The compound formed reduced Fehling's solution readily. It was not very basic in character.

Calculated for $C_9H_{13}O_2NHOH$, N = 7.45 per cent.

0.1067 gram substance 7.3 cc. N(22°, 748 mm.)

Found (corrected) N = 7.62 per cent.

The product, from its behavior toward Fehling's solution and its nitrogen analysis tended to show that it was the hydroxyl-amino derivative. It closely resembled Schryver's[1] hydroxylamino-lactone.

Action of ammonium hydroxide on the nitro isocampholactone.

Formation of an amide.

0.2 gram of the nitro-compound was dissolved in 10 cc. absolute alcohol and dry ammonia gas lead into it until a distinct odor of free ammonia became noticeable. It was then heated for 3 hours in a sealed tube on the water-bath, the tube opened and the product poured into an evaporating dish and allowed to go down in a vacuum desiccator over sulphuric acid. The resulting crystals were very difficultly soluble in ether, insoluble in petroleum ether, and very soluble in benzene. After recrystallization from benzene and the addition of a few drops of petroleum ether, the crystals melted between 96 - 97°.

0.2 gram nitro-compound was put in 10 cc. of concentrated ammonium hydroxide. This was shaken frequently and allowed to stand until all of the nitro compound was in solution. Upon allowing the ammoniacal solution to evaporate quickly in a current of air the same 96° melting product was obtained. This method yields better results.

---

1. J. Chem. Soc., 73, 562 (1898).

Calculated for $C_6H_{10}N_2O_3$, C = 45.57, H = 6.3, N = 17.71 per cent.

Found

0.1024 gram substance gave 0.1717 gram CO_2, 0.064 gram H_2O,

C = 45.7 per cent., H = 7.0 per cent.

0.1090 gram substance gave 0.1822 gram CO_2, 0.0689 gram H_2O,

C = 45.6 per cent., H = 7.06 per cent.

0.1024 gram substance gave 0.1721 gram CO_2, 0.0653 gram H_2O,

C = 45.8 per cent., H = 7.14 per cent.

0.1028 gram substance gave 16.4 cc. N at 20.40 and 743.5 or 17.6 per cent.

0.0753 gram substance gave 12.0 cc. N at 22.0 and 744.5 or 17.6 per cent.

0.1127 gram substance gave 16.5 cc. N at 17.5 and 746.0 or 16.6 per cent.

Saponification of the amide with sodium hydroxide. Formation of an acid.

0.1 gram of the amide, $C_6H_{10}N_2O_3$, was placed in a tube with 10 cc. N/2 sodium hydroxide and the tube sealed and heated on the water-bath for 12 hours. Upon heating the tube no pressure could be detected, however, a strong formaldehyde odor was evident. The solution was made strongly acid, whereupon it turned blue. The acid solution was extracted repeatedly with ether. The ether was evaporated off and the residue dissolved in as little water as possible and barium carbonate slowly added until effervescence ceased. This was then filtered and the clear solution allowed to evaporate spontaneously. The crystals formed were dried and gave the following analysis:-

0.0540 gram of anhydrous Ba salt gave 0.0255 gram $BaSO_4$ or 30.34 o/o Ba

0.1049 gram of anhydrous Ba salt gave 0.0492 gram $BaSO_4$ or 30.40 o/o Ba

0.1049 gram of anhydrous Ba salt gave 0.0101 gram H_2O or 9.62 o/o H_2O

0.0681 gram of anhydrous Ba salt gave 0.0067 gram H_2O or 9.83 o/o H_2O

Calculated for $(C_6H_8NO_4)_2Ba$, Ba = 30.30.

$(C_6H_8NO_4)_2Ba, 2\ 1/2\ H_2O = H_2O$= 9.03 per cent.

The free acid was liberated from the barium salt and melted at 73°. It was a white camphor-like solid, readily soluble in benzene but did not crystallize thereform. It was insoluble in ligroin. The acid was thrown down as a syrupy mass from the benzene with ligroin.

Hydrolysis of the amide with hydrochloric acid.

0.2 gram of the amide was put in a tube and 10 cc. N/2 hydrochloric acid added. The tube was sealed and heated on the water-bath for 18 hours, when it was cooled and the liquid extracted with ether. The ethereal solution was washed with water, leaving an oily residue after the ether had been evaporated. This residue was acid in character and was taken up in ammonium hydroxide, the excess of NH_3 driven off and the silver salt prepared.

Analysis:-

0.0169 gram substance gave 0.0103 gram after ignition or 60.09 per cent Ag

Calculated for $C_4H_8\begin{matrix}COOAg\\COOAg\end{matrix}$ - Ag = 60.00 per cent.

The analysis conformed to the silver salt of adipic acid. From this analysis it would seem that the amide upon hydrolysis with hydrochloric acid lost both nitrogens.

Titration of the nitro-isocampholactone with N/2 NaOH.

0.1875 gram of the product were put into exactly 5 cc. N/2 sodium hydroxide and allowed to stand 17 hours, after which it was all in solution. It was then titrated with N/10 hydrochloric acid. To get to the first neutral point it took 7.45 cc. It afterward became alkaline again and acid was added in quantities of 1.5 cc. every 10 minutes. After two hours the alkalinity returned very slowly, so that after 5 hours standing the acidity seemed to remain constant. Up to this point 14 cc. had been added. Three cc. more of N/2 sodium

hydroxide were added and allowed to stand over night and again titrated in the morning. This time it took 9 cc. of the N/10 acid to bring it to the neutral point. The alkalinity, however, returned rapidly and the acid was again added successively as before. As will be noted from the above the peculiar behavior of the end point did not lead to anything definite. Up to the first end point required 1.88 cc., whereas only 1.65 cc. were used.

Treatment of nitro-isocampholactone with sodium hydroxide.

Formation of an acid.

1 gram of the nitro-isocampholactone was dissolved in 30 cc. of N/2 sodium hydroxide. This was allowed to stand until it was all in solution and then filtered from suspended particles. Then it was neutralized with 1 : 1 hydrochloric acid and extracted four times with ether. The ethereal solution was dried with sodium sulphate and the ether evaporated off. An oily substance remained which weighed 0.7 gram. Upon cooling, it solidified. The product was dissolved in water and pure barium carbonate added slowly until effervescence ceased. It was filtered from the excess barium carbonate and set in a vacuum desiccator over sulphuric acid. A beautiful crystalline salt separated. The salt was filtered from the solution and washed twice with water. It was then dissolved in as little water as possible and acidified with 1 : 1 hydrochloric acid and extracted with ether. The ethereal solution was dried with sodium sulphate and after decantation the ether allowed to evaporate in a rapid current of air, and then set in a vacuum desiccator over sulphuric acid for 24 hours. The resulting product melted between 73° and 74°. The acid was very soluble in benzene, insoluble in ligroin. When a few drops of ligroin were added to the acid in benzene it precipitated as a thick pasty mass. The analyses of the free acid were not very satisfactory, due probably to a decomposition of it. Since allow-

ing it to stand in the air, the acid gradually became semi-solid and the analyses made on the product which had stood were very unsatisfactory.

Calculated for $C_8H_9NO_4$, C = 45.2, H = 5.66, N = 8.8 per cent.

Found

I 0.1065 gram substance gave 0.1777 gram CO_2, 0.0564 gram H_2O,

C = 45.6 per cent, H = 5.9 per cent.

0.1299 gram substance gave 0.2187 gram CO_2, 0.0738 gram H_2O,

C = 45.8 per cent. H = 6.35 per cent.

0.1305 gram substance gave 9.1 cc. at 17.5° and 741.0 mm.

or N = 7.8 per cent.

II 0.0948 gram substance gave 0.1597 gram CO_2, 0.057 gram H_2O,

C = 45.8 per cent, H = 6.4 per cent.

0.1177 gram substance gave 7.7 cc. at 16.5° and 742.0 mm.

or N = 7.5 per cent.

Titration of the acid.

	I	II
Gram of substance used	0.0519	0.0529
Number of cc. N/10 NaOH =	3.187	3.239
Molecular weight	162.9	163.0

In these titrations the first end point was sharp. After this, however, it became alkaline again.

A second titration was tried with barium hydroxide. 0.05 gram of the nitro-isocampholactone was put in a tube and 10 cc. of barium hydroxide added. (1 cc. barium hydroxide = .0049). The tube was heated for 12 hours, then opened and still found acid. 8 cc. more of barium hydroxide were added, 1.95 cc. being required to neutralize the solution. The tube was again sealed, and heated 8 hours more, cooled and titrated again. This time 0.3 cc. N/1 hydrochloric

acid was required to produce neutralization.

Total barium hydroxide used 12.05 cc. or 6.025 cc. N/10

∴ molecular weight either 83 or 166.

An attempt was made to find out whether any carbon dioxide was split off in the saponification of the nitro-isocampholactone with the sodium hydroxide. To do this 1 gram of the nitro-compound was put into an eight inch test tube and 30 cc. of sodium hydroxide added.

Air which had been dried and freed from carbon dioxide was sucked through this sodium hydroxide solution and lead into a solution of barium hydroxide. Gradually a precipitate of barium carbonate formed in the test tube. To make sure that the carbon dioxide came from the decomposition of nitro compound a blank of the sodium hydroxide used was run in a similar manner and no precipitate was obtained. Then another sample of the sodium hydroxide with a little sodium carbonate therein was run in like manner and a precipitate formed. It is evident from the above that carbon dioxide was aplit off in the saponification of the nitro-isocampholactone.

Phenyl hydrazine has no effect on the acid at all.

Acetyl chloride, when warmed with the acid on the water-bath for an hour and then allowed to evaporate off spontaneously, yielded a product which melted at 95 - 96°. When recrystallized from benzene and petroleum ether it melted at 100°.

Dissolving the acid in ammonium hydroxide and allowing the solution to evaporate yielded a product which melted at 144°, recrystallizing from alcohol yielded a product which melted at 148 - 149°.

Barium salt of the acid, $C_6H_9NO_4$.

The acid as obtained on page 24 was taken up in as little water as possible and barium carbonate added until the effervescence ceased. It was then filtered from the excess barium carbonate and allowed to evaporate spontaneously. A beautiful crystalline product formed. This was filtered from the mother liquor and washed several times with a small quantity of cold water. The crystals after air drying over night gave the following results:-

0.1045 gram substance air dried 5 hours gave 0.0116 moisture and
0.0479 gram $BaSO_4$ or 11.1 per cent. moisture and 30.34 per cent. Ba
0.1056 gram at 75° lost 0.0102 gram moisture and gave
0.0491 gram $BaSO_4$ or 9.67 per cent. moisture and 30.27 per cent. Ba
0.3111 gram at 80° lost 0.0303 gram moisture or 9.73 per cent.
0.456 gram at 90° lost 0.0444 gram moisture of 9.73 per cent.
The last two were first air dried for 24 hours.

Combustion of barium salt (Potassium dichromate method).
0.1018 gram substance gave 0.1093 gram CO_2, 0.0438 gram H_2O, or
29.2 per cent. C, 4.8 per cent. H.
0.1113 gram substance gave 0.1185 gram CO_2, 0.0476 gram H_2O, or
29.0 per cent. C, 4.7 per cent. H.
0.0985 gram substance gave 5.1 cc. N at 20° and 743.5 mm. or
6.38 per cent. N.
Calculated for $(C_6H_8NO_4)_2Ba \cdot 2H_2O$, C = 29.4, H = 4.09, N = 6.12
Calculated for $(C_6H_8NO_4)_2Ba \cdot 2\ 1/2\ H_2O$, C = 28.9, H = 4.2, N = 6.12

The calcium salt of this acid was formed just as easily as the barium salt. The crystals, however, were not so well defined. It is more difficult to

determine the per cent. of moisture in the calcium salt due to its explosive character.

Second product obtained by the oxidation of the iso-camopholactone.

The liquid obtained during the oxidation of the isocampholactone and from which the crystals of nitro-isocampholactone had been filtered was evaporated down to dryness on the water-bath. Water was added repeatedly and evaporated down several times in order to get rid of all the nitric acid. The residue was then set in a vacuum desiccator over sulphuric acid and after 24 hours the thick jelly-like mass became crystalline. This was pressed on a porous plate and allowed to dry, and then recrystallized from benzene. After two recrystallizations the crystals melted at 138°. These crystals were insoluble in ligroin, soluble in absolute alcohol from which they crystallized in long fern-like crystals.

Titration of the product:-

0.0517 gram required 2.779 cc. N/10 NaOH or molecular weight 186.0

0.0527 gram required 2.821 cc. N/10 NaOH or molecular weight 186.8

Analysis:-

Product recrystallized twice from benzene.

0.1062 gram substance gave 0.2301 gram CO_3, 0.0689 gram H_2O,

C = 59.09 per cent., H = 7.2 per cent.

Product recrystallized six times from benzene

0.1022 gram substance gave 0.2231 gram CO_2, 0.064 gram H_2O

C = 59.5 per cent., H = 7.02 per cent.

Product recrystallized eight times from benzene

0.1063 gram substance gave 0.2300 gram CO_2, 0.0683 gram H_2O

C = 59.00 per cent., H = 7.20 per cent.

Calculated for $C_9H_{14}O_4$, C = 58.06, H = 7.52.

The results obtained were too high which was probably due to a solid solution of the isocampholactone with the acid.

Rotation $[\alpha]_D = -42^\circ.05$

Preparation of barium salt of the acid $C_9H_{14}O_4$ with barium carbonate.

0.1 gram of the 138° product was dissolved in water. To this aqueous solution pure barium carbonate was added until effervescence ceased. The excess of barium carbonate was then filtered off and the liquid allowed to evaporate spontaneously. A crystalline body formed. This was very readily soluble in water. The crystals showed no water of crystallization.

0.0758 gram of the barium salt gave 0.0349 gram $BaSO_4$ or Ba = 27.04 per cent.

Calculated for $(C_9H_{13}O_4)_2Ba$, Ba = 27.02 per cent.

Preparation of barium salt of the acid $C_9H_{14}O_4$ with barium hydroxide.

0.1 gram of the 138° product was heated on the water-bath for 4 hours with 2 1/2 equivalents of barium hydroxide. After this a rapid current of carbon dioxide was passed through the solution in order to get rid of the excess of barium hydroxide. It was then warmed to drive off all the carbon dioxide. The solution was then filtered and allowed to go down gradually; long, brittle, and silky needle-shaped crystals forming.

0.096 gram of the salt gave 0.0568 gram $BaSO_4$, or Ba = 37.8 per cent.

the salt lost only 0.0065 gram H_2O at 120° or 0.67 per cent.

Titration for the detection of the lactone group.

0.0569 gram of the 138° substance was treated with 12.95 cc. of N/10 sodium hydroxide. This was placed in a test tube, closed with a rubber-stopper and heated on the water-bath for 12 hours, allowed to cool and then titrated with N/10 hydrochloric acid. 6.37 cc. N/10 NaOH were used to saponify the .0569 gram. 0.0569 gram requires 3.05 cc. N/10 NaOH.

For two carboxyls it would require 6.10 cc. N/10 NaOH,

used 6.37 cc. N/10 NaOH.

Treatment of the 138° product ($C_9H_{14}O_4$) with phosphorus pentachloride.

0.5 gram of the 138° product was placed in a test tube and mixed with five times its weight of phosphorus pentachloride. The test tube was closed with a "Wallach's Aufsatz", and the mixture slowly heated over the free flame, until the mass was liquid and remained so. This was then allowed to cool and poured into ammonium hydroxide which had some mashed ice in it. A crystalline solid separated at once. Upon filtering and drying, it showed a melting-point of 164°.

0.105 gram gave 7.5 cc. at 23° and 741 mm. or N = 7.84 per cent.

Calculated for $C_9H_{13}O_3NH_2$, N = 7.57 per cent.

Treatment of the 138° product ($C_9H_{14}O_4$) with ammonium hydroxide.

0.2 gram of the acid, $C_9H_{14}O_4$, was heated 18 hours on the water-bath in a sealed tube with 10 cc. of concentrated ammonium hydroxide. Then cooled

and some of the ammonia evaporated off; the liquid was then acidified and extracted with ether repeatedly. After the evaporation of the ether the original 138° product was left. Evidently no NH_2 group had entered.

In the study of the products of oxidation, in addition to the 122° melting product, the nitro-isocampholactone, and the 138° melting product, the acid, there were two other products, which, however, were obtained in such small quantities that no identification of them could be made. On allowing the mother liquor from the oxidation to stand, a crystalline body deposited in light plates. These melted at 111°, they do not dissolve in sodium carbonate, nor ligroin, but dissolve readily in chloroform, ether, acid water. Upon extracting with ether the mother-liquor after filtering off the 111° crystals, a very small amount of a compound was obtained, which melted at 226°. This same product was obtained when the mother-liquor was completely diluted with water. It then falls down as a light precipitate. This, the 226° product, dissolves in warm chloroform, in acetic acid and readily in ether. Recrystallized from ligroin it melts at 228°. The product is soluble in sodium carbonate. The color produced by adding a drop of bromine to its solution in chloroform is not discharged nor is the solution of it in sodium carbonate decolorized by potassium permanganate unless warmed.

So far I have been unable to determine the conditions under which the above products formed. They were, however, obtained from two different lots and under entirely different conditions. The yields in both cases were very poor and therefore no further work could be carried out therewith.

SUMMARY.

1. The method of purifying the hydrochloride of aminolauronic acid was improved.

2. A new method for the preparation of the ethyl ester of aminolauronic acid from the aminolauronic acid hydrochloride was worked out.

3. An analysis was made and a rotation taken of the hydroxylauronic ester, $C_8H_{14}(OH)CO_2C_2H_5$. The rotation was taken of the γ-lauronolic ester, $C_8H_{13}CO_2C_2H_5$.

4. The copper salt of the hydroxy acid, $(C_8H_{14}\begin{matrix}CO_2\\OH\end{matrix})_2Cu + 2H_2O$, was prepared and analysed.

5. The ester, $C_8H_{14}(OH)CO_2C_2H_5$, was treated with Beckmann's mixture and a ketone test obtained with phenyl hydrazine.

6. The hydroxy acid, $C_8H_{14}\begin{matrix}COOH\\OH\end{matrix}$, was oxidized with nitric acid, camphoronic acid was obtained as the principal oxidation product and a minute quantity of a product melting at 171°, possibly a nitro compound.

7. A new method was worked out for liberating the free aminolauronic acid from its hydrochloride.

8. A new method was worked out for the preparation of the isocampholactone from the nitroso-compound.

9. The isocampholactone was treated with ammonium hydroxide with the formation of the ammonium salt of the hydroxy acid, $C_8H_{14}\begin{matrix}COONH_4\\OH\end{matrix}$.

10. The isocampholactone was oxidized with nitric acid. Nitro-isocampholactone, $C_9H_{13}O_2NO_2$, - an acid, $C_9H_{14}O_4$, - small quantities of a 111° product (probably a lactone) insoluble in sodium carbonate, and of a 228° product (probably camphoronic acid) soluble in sodium carbonate were the oxidation products.

11. The action of phosphorus trichloride and pentachloride was tried on the nitro-compound.

12. The nitro-isocampholactone was reduced with zinc dust and glacial acetic acid, with the formation of a hydroxylamine derivative, melting at 142°.

13. The nitro-isocampholactone was reduced with tin and hydrochloric acid with the formation of amino isocampholactone, melting at 84°.

14. The nitro-isocampholactone was treated with (1) ammonium hydroxide and (2) with absolute alcohol and dry ammonia, with the formation of an amide, $C_6H_{10}N_2O_3$, melting between 96°- 97°.

15. The amide, $C_6H_{10}N_2O_3$, was saponified with sodium hydroxide; an acid, $C_6H_9NO_4$, melting between 73 - 74° was formed. The barium salt of the acid was prepared.

16. The amide, $C_6H_{10}N_2O_3$, was hydrolyzed with hydrochloric acid and the silver salt of the adipic acid formed prepared.

17. The nitro-isocampholactone was treated with sodium hydroxide with the formation of an acid, $C_6H_9O_4$, melting at 73°. This acid was identical with that obtained by the saponification of the amide.

18. The barium salt, $(C_6H_8NO_4)_2Ba \cdot 2\ 1/2\ H_2O$, was prepared from the acid, $C_6H_9NO_4$, with barium carbonate.

19. The barium salt, $(C_9H_{13}O_4)_2Ba$, was prepared from the 138° melting acid, $C_9H_{14}O_4$, with barium carbonate.

20. The preparation of a barium salt of the 138° acid, $C_9H_{14}O_4$, with barium hydroxide was tried.

21. The 138° acid, $C_9H_{14}O_4$, was warmed with sodium hydroxide and titrated; it showed the presence of a lactone group.

22. The $\underline{NH_2}$ group could not be made to enter the 138° acid even upon heating it with ammonium hydroxide in a sealed tube.

23. The 138° acid, $C_9H_{14}O_4$, was heated with phosphorus pentachloride and the product formed poured into cold ammonium hydroxide with the formation of an amide $C_9H_{13}O_2NH_2$ melting at 164°.

Biographical.

The writer received his early education in the schools of Sauk City, Wisconsin, graduating from the high school at that place in 1899. During the two years following he taught languages in the Denzer schools and in the fall of 1901 entered the University of Wisconsin, taking the degree of Bachelor of Arts in 1905 with "The Honors" in chemistry. During the next two years he was instructor in chemistry in the Rose Polytechnic Institute at Terre Haute, Indiana. In the fall of 1907 he received a fellowship in chemistry in the University of Illinois, taking the degree, Master of Arts, the following spring. In the fall of 1908 he entered the University of Göttingen, Germany, where he did research work for one year, again entering the University of Illinois on a fellowship in 1909.

He has published the following papers:-

"The Quantitative Estimation of Tellurium", with Dr. Victor Lenher.

"Molecular Rearrangements in the Camphor Series", with Dr. W. A. Noyes.

"Ueber Isofenchone", with Dr. Otto Wallach.

He is a member of the Alpha Tau Omega Fraternity, Gamma Alpha Research Fraternity, Phi Lambda Upsilon Fraternity and Die Burschenschaft Germania (Germany). He is also a member of the American Chemical Society, the Illinois Academy of Science and Die deutschen chemischen Gesellschaft.

UNIVERSITY OF ILLINOIS-URBANA
3 0112 086826614